Allergology International. 2013;62:391-393
DOI: 10.2332/allergolint.13-LE-0554

Dear Editor

Correlation between Soluble Interleukin-2 Receptor Levels and Modified Rodnan Total Skin Thickness Scores in a Patient with Generalized Morphea: A Case Report

Generalized morphea is a rare condition in which idiopathic sclerosis of the skin occurs in a widespread manner. It usually starts on the trunk and is not associated with systemic disturbances.[1] Interleukin-2 receptor (IL-2R) is a membranous glycoprotein that forms the high-affinity IL-2 receptor. The soluble form (sIL-2R) is elevated in most proliferative disturbances of the hematopoietic system and in many solid tumors.[2] Here, we describe in detail a correlation between soluble IL-2R levels and modified Rodnan total skin thickness scores (mRTSS) in a patient with generalized morphea treated with topical corticosteroids.

A 79-year-old Japanese woman was referred to our department for diagnosis of sclerotic skin with erythema on the chest, abdomen, waist, and right lower leg (Fig. 1a). The sclerotic skin of the abdomen had a 5-month history and the symptoms gradually spread to the chest, waist, and right lower leg. She had no medical history of note. Her younger sister had died due to collagen disease, but the patient did not know the accurate diagnosis.

Laboratory tests, including complete blood cell count, urinalysis, erythrocyte sedimentation rate, and liver and kidney functions were within normal limits. However, % eosinophils (12.0%; normal, 0-8%), lactate dehydrogenase (LDH) (288 IU/l; normal, 114-243 IU/l), and serum sIL-2R (1690 U/ml; normal, 145-519 U/ml) were elevated. Immunoglobulin (Ig) A, IgM, IgG and complement component 3 (C3) levels were within normal limits, but C4 (38.6 mg/dl; normal, 12-35 mg/dl) and total hemolytic complement (CH50) (63.0 U/ml; normal, 34-49 U/ml) levels were slightly elevated. Autoantibody screening was positive for

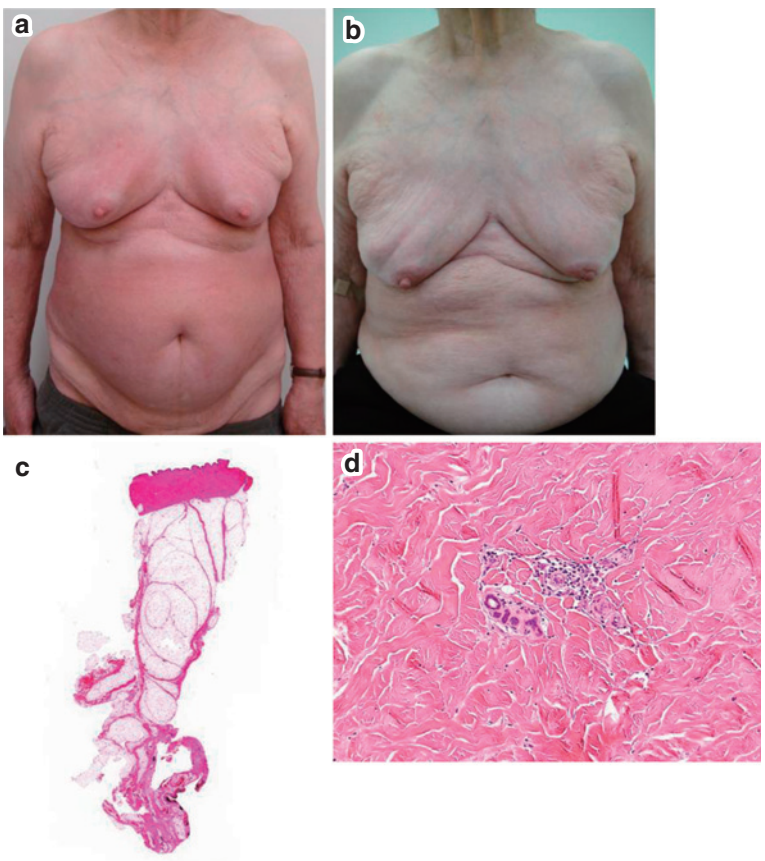

Fig. 1 Clinical photographs (**a**) at the first visit and (**b**) 21 months after starting treatment (remission). (**c**, **d**) Histological findings in hematoxylin and eosin-stained sections were consistent with scleroderma (original magnification: **c**, ×1; **d**, ×100).

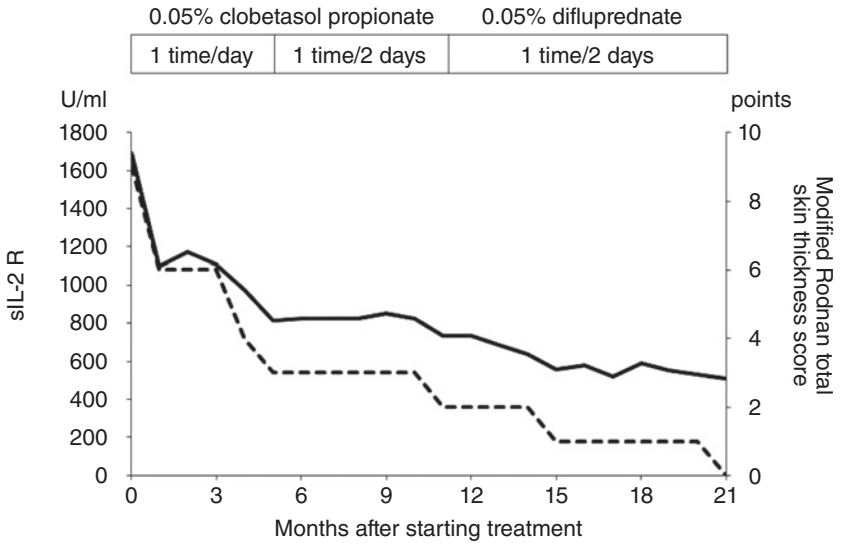

Fig. 2 Clinical course. Administered drugs are shown in the upper part of the figure and changes in clinical data are shown in the lower section. Soluble interleukin-2 receptor (sIL-2R, straight line) levels and modified Rodnan total skin thickness scores (mRTSS, dotted line) are shown on the left and right axes, respectively.

rheumatoid factor (18.5 IU/ml; normal, 0-15 IU/ml) and antinuclear antibody (titer, 1 : 80; normal, <1 : 40) with a speckled and homogenous pattern, and negative for anticentromere antibody and antitopoisomerase I antibodies. The serum level of Krebs von den Lungen-6 was also within the normal limit.

Chest radiography and computed tomography findings were normal. Pulmonary function tests and data from electro- and echocardiograms were also within normal limits. Normal esophageal peristaltic function was detected by esophagography with barium contrast medium. Gastrointestinal endoscopy and colonofiberscopy were also normal, but magnetic resonance imaging of the abdomen showed inflammation of the fascia.

These results suggested that the diseased area was limited to the skin (no systemic involvement), leading to suspicion of generalized morphea or eosinophilic fasciitis. Therefore, a skin biopsy including the fascia from the abdomen was performed to discriminate between these two diseases. The biopsy specimen showed thickened collagen bundles in the dermis, the septum of subcutaneous fatty tissue, and the fascia (Fig. 1c). Fatty tissues around the secretory portion of eccrine glands were replaced by thick fibrous bundles and the eccrine glands were atrophic (Fig. 1d). Eosinophilic infiltration was not found in the fascia. Based on these results, the patient was diagnosed with generalized morphea. Because of rapid progression of skin sclerosis, oral therapy with corticosteroids was recommended, but she chose topical corticosteroid therapy due to her anxiety about possible systemic side effects.

The mRTSS before treatment was 9. Once-daily topical application of 0.05% clobetasol propionate ointment was started and within 5 months the mRTSS had improved to 3 and serum sIL-2R was reduced to 817 U/ml (Fig. 2). Topical application of 0.05% clobetasol propionate ointment was continued at a reduced frequency of once every two days and within 11 months after the start of treatment the mRTSS had improved to 2 and serum sIL-2R to 732 U/ml. At this time, the treatment was switched to a weaker topical steroid (0.05% difluprednate applied once every two days). Within 21 months after the start of treatment, the mRTSS had a normal value of 0 and the serum sIL-2R level had similarly normalized at 509 U/ml, respectively. The patient has subsequently been in remission for a further 6 months (Fig. 1b).

sIL-2R levels in patients with systemic sclerosis and localized scleroderma have been reported to be correlated with disease severity and treatment efficacy.[3-6] Uziel *et al*. described elevated sIL-2R levels in patients with linear scleroderma in the active phase (new lesions, increased size of existing lesions, or erythematous lesions) compared to the inactive phase (no new lesions and softening and brownish discoloration of the skin). However, the current report described in detail correlations among the efficacy of treatment, mRTSS, and serum level of sIL-2R in a case of generalized morphea. Our case was in the active phase of generalized morphea based on the natural clinical course before treatment, and mRTSS and serum sIL-2R decreased from 9 to 0 and 1690 to 509 U/ml, respectively, which clearly correlated with recovery from the disease.

Recently, cytokine network consisting of IL-17A and IL-23 is considered related to the pathogenesis of

scleroderma,[7-9] but the measurement of these cytokine levels may still not be realistic indication. High resolution B-mode ultrasound is helpful for evaluating treatment efficacy, but the measurement has poor reproducibility unless it is performed under the same conditions by the same operator. Histopathological examination by skin biopsy is the most reliable method for evaluation of treatment efficacy, but it is invasive and our patient refused a skin biopsy during the treatment course. In contrast, measurements of the mRTSS and serum level of sIL-2R are safe and simple, and thus may be especially useful for monitoring disease severity and the response to treatment in patients with generalized morphea.

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Conflict of interest: No potential conflict of interest was disclosed.

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